

## **REMARKS**

Claims 1 and 3-27 and 32 are pending.

In a February 11, 2003 final action, claims 1, 3-27, and 32 were rejected on various grounds including 35 U.S.C. § 112 first and second paragraphs and § 103(a). Reconsideration and withdrawal of the rejections are respectfully solicited in view of the foregoing amendments and the following remarks.

### **I. EXPLANATION OF AMENDMENTS TO THE CLAIMS**

Support for the amended and new claims is found throughout the specification. The present amendment introduces no new matter.

A number of amendments to the claims, *e.g.* 1 and 32, have been made merely to improve or clarify the English grammar, or to establish proper antecedent basis. The only substantive changes occur in claims 1 and 32, and even in those claims not all changes are of a substantive nature. The term "homogeneous" has been removed, the addition of this term having been rejected in the February 11, 2003 action. The term "porous" has been added to describe the cell culture insert, finding support, for example, on page 5, lines 32-33. The term "sustained" has been added to describe the culture medium supply conditions, finding support, for example, on page 15, lines 1-8. Additional descriptive language had been added to describe the basal culture medium supply condition, but this change does not affect the scope of the claims as the meaning of basal medium supply condition remains unchanged. Throughout the claims, the removal of the phrase "at least one" does not indicate or imply that a particular claim no longer encompasses embodiments where there are more than one of a particular element or sub-element. The applicants do not intend by these or any other amendments to abandon the subject matter of any claim as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

### **II. APPROVAL OF THE DRAWINGS**

In paragraph 6, the examiner stated the approval of the proposed drawing correction and/or proposed substitute sheets of drawings filed on November 15, 2002. As required, formal drawings including all approved changes are submitted herewith in a separate document entitled "Submission of Substitute Formal Drawings."

### **III. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, HAS BEEN RENDERED MOOT BY THE PRESENT AMENDMENT**

In paragraph 8, claims 1 and 3-27 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter that was not described in the specification. Specifically, the action stated that the use of the term "homogenous" in respect to particulates in claim 1 did not find support in the specification. The applicants disagree, but believe that the rejection has been rendered moot. Claim 1 as amended does not recite the term "homogenous." Accordingly, the rejection should be withdrawn.

### **IV. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, IS MOOT AND SHOULD BE WITHDRAWN**

In paragraph 10, claims 1 and 3-27 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Specifically, in paragraph 11, the action stated that the limitation "the cultured cells" in line 13 of claim 1 (before amendment) lacked sufficient antecedent basis. The applicants believe that this rejection has been rendered moot by the present amendment. Accordingly, the rejection should be withdrawn.

### **V. THE REJECTION UNDER 35 U.S.C. § 103 SHOULD BE WITHDRAWN AS THE PRIOR ART FAILS TO RECITE ALL THE CLAIM ELEMENTS**

In paragraph 13, claims 1, 3-27 and 32 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Pat. No. 5,424,209 (Kearney) in view of SU 734281B (Pankratove, *et al.*), JP 402119772 (Hamazaki) and GB 2314343A (Liau). The applicants respectfully traverse this rejection because the official action has failed to establish a *prima facie* case of obviousness.

In order to establish a *prima facie* case of obviousness, the prior art reference (or references when combined) cited by the examiner must teach or suggest all the claim limitations. *See* M.P.E.P. § 2143.03: "All the words in a claim must be considered in judging the patentability of that claim against the art." As amended, claims 1 and 32 recite a **porous** cell culture insert providing a **horizontal** culture surface. Claims 1 and 32 also recite "a sustained basal culture medium supply condition." Additionally, both claim 1 and 32 recite a device that "can achieve both a sustained submerged culture medium supply condition and a sustained basal culture medium supply condition." None of the cited references teach or suggest such elements.

**None** of the references cited teaches or suggests a porous, horizontal cell culture insert or a basal supply condition. Moreover, without a porous, horizontal insert, a

"basal culture medium supply condition" cannot be achieved. Such a basal condition allows for a substantial number of cells to be in simultaneous contact with cell culture medium from below, and gases, aerosols, and/or particulate matter from above. *See, e.g.*, the specification at page 6, lines 29-34, and claims 1 and 32. The combination of cited references fails to disclose a basal supply condition. Without a porous cell culture insert, the culture cannot reach the underside of the cells mounted on the cell insert. The combination of cited references fails to disclose at least a porous, horizontal insert and a basal supply condition.

For example, Kearney reports that cells can be grown directly on slides or coverslips, at column 21, line 26 of the '209 patent. While slides and coverslips may represent horizontal cell culture inserts, they are **not porous**. It is understood by those of ordinary skill in the art that slides and coverslips are impermeable barriers. Kearny confirms this understanding, because it states that if one wishes to use slides and/or coverslips to grow cells, then one must use "hollow fiber techniques," because it is the use of such techniques that allow the cells to grow. *See* column 21, lines 24-26. If Kearney taught porous, horizontal cell culture inserts, such techniques would not be necessary. Further, as the action admits, Kearney does not teach a basal medium supply condition. Again, "all the words in a claim must be considered." Accordingly, Kearney does not teach at least these necessary limitations of the claims.

The description of the references provided in the official action establishes that none of the other cited references teach or suggest a "sustained basal culture medium supply condition." A basal condition allows for a substantial number of cells to be in simultaneous contact with cell culture medium from below, and gases, aerosols, and/or particulate matter from above. Each of the references, as admitted in the action, teaches instead only "**periodic exposure**" of cells to either culture media (submerged condition) or gasses (non-basal condition) by "**changing**" the level of the culture medium. Moreover, it is specifically admitted in the action that "Kearney did not teach...a basal medium supply condition."

Pankratov et al., page 5 of SU 734281B, teach a device that contains two vessels such that nutrient medium is switched from one vessel to another so that cells in one vessel are submerged while the cells in the other are not. However, Pankratov et al. do not teach a sustained basal medium supply condition. Hamazaki, pages 3-6 and 12-13 of JP 402119772, teaches a cell culturing device consisting of various sensors and mechanisms for regulating cell density and the amount of culture solution, but does not teach a basal medium

supply condition. Liao, pages 5-7 of GB2314343A, teaches submerging and exposing a cell anchorage surface, but does not teach a basal medium supply condition. The cited references fail to teach a sustained basal medium supply condition, a feature of claims 1 and 32.

Accordingly, the rejection should be withdrawn. In contrast, each reference teaches only changing a level of the liquid medium between a submerged supply condition and a condition where cells are not in contact with the supply of liquid medium.

The official action (third paragraph) states on page 7 that one of ordinary skill would have been motivated to combine the teachings of Kearney, Pankratov et al., Hamazaki and Liao to achieve the desirable and beneficial cell growth advantage of changing between a submerged and a "low culture" medium level. Without addressing whether the stated "motivation" is legally sufficient, such a combination does not produce the presently-claimed invention, because the cited references do not comprise all the claim limitations as discussed above. The prior art cannot suggest the desirability of a combination of elements if the prior art does not each all of the elements. Here, the cited references do not teach or suggest the desirability of simultaneously exposing cells to both cell medium and gasses (*i.e.*, a basal condition) without changing the level of culture medium. "The level of skill in the art cannot be relied upon to provide the suggestion to combine references." M.P.E.P. § 2143.01.

The present invention provides a novel, nonobvious device having a number of features and capabilities including using a porous, horizontal insert to allow for a sustained basal culture medium supply condition that achieves simultaneous exposure of cells to cell medium and gasses without changing the level of the medium. That the claimed device is capable of changing the medium level, *e.g.* to a submerged condition, does not detract from the novel, non-obvious features and capabilities of the claimed device.

None of the cited references teach or suggest, alone or in combination, a device capable of a sustained basal culture medium supply condition, as clearly defined in the present application. None of the cited references teach or suggest, alone or in combination, a porous, horizontal cell insert, as clearly defined in the present application. None of the cited references teach or suggest, alone or in combination, a device capable of achieving both a sustained submerged culture medium supply condition and a sustained basal culture medium supply condition. Accordingly, and for all the reasons discussed above, a *prima facie* case of obviousness has not been established and the rejection of the claims under 35 U.S.C. § 103(a) should be withdrawn.

### CONCLUSION

The applicants respectfully request prompt reconsideration of the pending claims. Claims 1, 3-27 and 32 are believed to be in condition for allowance in view of the foregoing amendments and remarks. Withdrawal of the rejections and allowance of the claims are respectfully solicited.

The examiner is invited to contact the undersigned at the telephone number listed below in order to discuss any remaining issues or matters of form that will move this case to allowance.

A petition and fee for a one-month extension of time accompany this paper. Thirty-one claims have previously been paid for, and by this paper, only two independent claims and 27 total claims are pending. Therefore, no additional fees are believed due. However, the Commissioner is hereby authorized to charge any fee deficiency, or credit any overpayment, to Deposit Account No. 13-2855 of the undersigned.

Respectfully submitted,

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